2019-nCoV Literature Situation Report (Lit Rep)
February 28, 2020

The scientific literature on COVID-19 is rapidly evolving and these articles were selected for review based on their relevance to Washington State decision making around COVID-19 response efforts. Included in these Lit Reps are some manuscripts that have been made available online as pre-prints but have not yet undergone peer review. Please be aware of this when reviewing articles included in the Lit Reps.

Key Takeaways

- **Testing methodologies continue to be evaluated for sensitivity and specificity, especially in relation to disease stage and severity. One new study found that the presence of viral RNA in blood and anal swabs is associated with severe disease.**
- **More studies seek to describe early clinical characteristics of patients to improve diagnostic accuracy. Some patients do not to present with fever and one study suggests that attending physicians should take this into consideration, particularly in outbreak areas.**
- **Determining how long patients continue to shed the virus after symptom recovery remains a focus of current research efforts. One new study found that patients can still test positive for the virus two weeks after clinical signs disappear.**
- **Two new studies add to the discussion around the potential of vertical transmission of COVID-19 during pregnancy, though findings across studies remain inconsistent.**

Clinical Characteristics and Health Care Setting

- Guan et al reviewed clinical data from 1,099 lab-confirmed COVID-19 patients in China. They describe their composite end points, human and animal contacts, clinical symptoms, and radiological and laboratory diagnoses. They report that patients often presented without fever at admission (56.2%) and hospitalization (11.3%) and many did not have abnormal radiologic findings, a tool primarily used in diagnosis of pulmonary changes. This is an important consideration for physicians managing and identifying patients.

  Guan et al. (Feb 28, 2020). Clinical Characteristics of Coronavirus Disease 2019 in China. The New England Journal of Medicine. https://www.nejm.org/doi/full/10.1056/NEJMoa2002032

- Rasmussen et al reviewed two reports describing 18 pregnant women with COVID-19 that were infected in the third trimester. They reported clinical findings were similar to those in non-pregnant adults. Fetal distress and preterm delivery were seen in some cases. All but two pregnancies were cesarean deliveries, and testing for SARS-CoV-2 was negative on all babies tested. They recommend close fetal and maternal monitoring and adherence to principles of COVID-19 management in pregnancy.

  Rasmussen et al. (Feb 28, 2020). Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know. American Journal of Obstetrics and Gynecology. https://doi.org/10.1016/j.ajog.2020.02.017

- Li et al (2020) conducted an investigation into the capacity of vertical transmission of SARS-CoV-2 using Angiotensin-converting enzyme 2 (ACE2), a confirmed receptor of SARS-CoV-2 that plays essential roles in human infection and transmission. They used an open source online single-cell RNA sequencing data, to evaluate the cell specific expression of ACE2 in maternal-fetal interface as well as in multiple fetal organs. Results revealed that ACE2 was highly expressed in maternal-fetal interface in the placenta and many fetal organs, suggesting the potential capacity for the infection of SARS-CoV-2 to the fetus through the vertical transmission.

  Li et al. (Feb 27, 2020). The ACE2 expression of maternal-fetal interface and fetal organs indicates potential risk of vertical transmission of SARS-COV-2. Pre-print downloaded Feb 28 from https://doi.org/10.1101/2020.02.27.967760

- An update by a radiology scientific expert panel in the US reviewed current COVID-19 diagnostic tools for limitations. They report that up to 50% of patients may have normal CT scans 0-2 days after onset, 50%-75% of patients may have lung abnormalities early in disease progression, and that RT-PCR sensitivity may be as low as 60-70%.

  Kanne et al. (Feb 27, 2020). Essentials for Radiologists on COVID-19: An Update—Radiology Scientific Expert Panel. Radiology. https://pubs.rsna.org/doi/10.1148/radiol.2020200527

- Four recovered patients with COVID-19 who met criteria for hospital discharge or discontinuation of quarantine in China were evaluated with RT-PCR tests for COVID-19 nucleic acid to determine if they could return to work. All had positive RT-PCR test results 5 to 13 days later which suggests a need to reevaluate current criteria for hospital discharge or discontinuation of quarantine and continued patient management.

  Lan et al. (February 27, 2020). Positive RT-PCR test results in patients recovered from COVID-19. JAMA Research Letter. https://jamanetwork.com/journals/jama/fullarticle/2762452

- Li et al developed a rapid and simple point-of-care lateral flow immunoassay to simultaneously detect IgM and IgG antibodies within 15 minutes from human blood, plasma, or serum collected at different stages of infection. Overall sensitivity of the combined test was 88.7% and specificity was 90.6% and had better utility and sensitivity than separate IgM or IgG tests. This new test is potentially applicable for rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic, in hospitals, clinics, and test laboratories.

  Li et al. (Feb 27, 2020). Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis. Journal of Medical Virology. Pre-print downloaded Feb 28 from https://doi.org/10.1002/jmv.25727

- In absence of FDA-approved antiviral therapies for COVID-19, Yao et al reviewed efficacy of Lopinavir (LPV), an agent used during SARS and MERS epidemic, to clarify its potential for use in patients with COVID-19. Currently a combination of LPV/r is a recommended treatment in China. They reported on two reviews; one with success on limited patients and bigger study with variable outcome. They call for more clinically valid evidence (RCT) to confirm the positive value of LPV for COVID-19 treatment. Adverse reaction including diarrhea, nausea, and asthenia were frequently reported among other symptoms.

  Yao et al. (Feb 27, 2020). A Systematic Review of Lopinavir Therapy for SARS Coronavirus and MERS Coronavirus–A Possible Reference for Coronavirus Disease-19 Treatment Option. Journal of Medical Virology. https://doi.org/10.1002/jmv.25729

- This case report describes a 28 year old patient diagnosed with pneumonia who initially tested negative for COVID-19 on nasopharyngeal and oropharyngeal (NP/OP) samples. The patient tested positive for SARS-CoV-2 by RT-PCR on broncho alveolar lavage (BAL) fluid on day 8 of hospitalization. This case highlights the importance of clinical suspicion in the epidemiologically-matched patients who have negative NP/OP swab.

  Kaewpoowat et al. (Feb 26, 2020). Negative Nasopharyngeal and Oropharyngeal Swab Does Not Rule Out COVID-19. Journal of Clinical Microbiology. https://www.ncbi.nlm.nih.gov/pubmed/32102856

- Chen et al analyzed virus presence using RT-PCR in blood and pharyngeal and anal swabs. They report that the presence of viral RNA in the blood and anal swab is positively correlated with the severe disease stage. They recommend that early monitoring of virus RNA in blood and the digestive tract on top of the respiratory tract might support better disease prediction.

  Chen et al. (Feb 26, 2020). Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity. Emerging Microbes & Infections. https://doi.org/10.1080/22221751.2020.173283.

Mental Health and Personal Impact

- A psychiatrist shares his experience working on the H1N1 pandemic in Japan to inform COVID-19 response efforts. He notes the stresses on healthcare providers, including physical exhaustion, anxiety about infection, and need for mental health support.
- A 2009 survey of 3,635 healthcare providers in Japan revealed that 28.4% felt motivated to work during the pandemic and 14.7% were very hesitant to work. Willingness to work was tied to feeling protected by national and local governments and by the hospital. Those most reluctant to work cited worries about infection, compensation, and feeling isolated. The author concludes that trust in organizations, frequent communication of information, and psychological support are key to *employee willingness to work and staff retention.*

  Imai (Feb 27, 2020). Trust is a key factor in the willingness of health professionals to work during the COVID-19 outbreak: Experience from the H1N1 pandemic in Japan 2009. Psychiatry and Clinical Neurosciences. https://doi.org/10.1111/pcn.12995

- A cross-sectional online survey was conducted only 36 hours after the first COVID-19 patient was confirmed in Hong Kong, and continued from Jan 24 to Feb 13. 1,715 people completed the survey on perceived health status, risk perception, information sources, travel history, respiratory symptoms in the previous 14 days.
- The most common information sources were social platforms (94%) and websites (90%), even though they were poorly rated in terms of reliability (16%-23%) and trustworthiness. Most respondents regarded themselves as likely to be infected (89%), and if infected, considered the severity to be serious (97%). Only 15% of respondents thought they would be likely to survive COVID-19 and considered severity to be lower than SARS. Anxiety rates were high, and enhanced personal hygiene and travel avoidance were adopted by most respondents. Social distancing was most common among women and those with more anxiety.
- Given the population's reliance on social media and online information, the authors suggest that scientific information be conveyed via those channels. In addition, the authors suggest that early recognition of perceived risk, combined with access to trusted sources of information as a way to enhance non-pharmaceutical interventions may assist other countries in the early stages of an outbreak.

Kwok et al. (Feb 27, 2020). Community responses during the early phase of the COVID-19 epidemic in Hong Kong: risk perception, information exposure and preventive measures. Pre-print downloaded Feb 28 from https://doi.org/10.1101/2020.02.26.20028217

- The authors describe an outbreak of COVID-19 at a state psychiatric inpatient hospital in Wuhan, China. Although the hospital closed the facility to visitors, there was widespread infection among the patients and staff. As of Feb 8, 2020 50 patients and 30 staff had been infected.
- The authors noted several elements that contributed to the complexity of the outbreak and that may be taken into consideration for planning and preparedness efforts among especially vulnerable institutionalized populations. The authors offer several recommendations to improve patient outcomes, support staff, and connect with families of patients

  Zhu et al. (Feb 25, 2020). The Risk and Prevention of Novel Coronavirus Pneumonia Infections Among Inpatients in Psychiatric Hospitals. Neuroscience Bulletin. https://doi.org/10.1007/s12264-020-00476-9

Want to get caught up? Try these reads…

- Rio and Malani provide new insights on a rapidly changing COVID-19 epidemic. The editorial updates previous guidance for clinicians, summarizes what is known, what is unknown, and what are the next steps based on available evidence to address and halt the outbreak. There are commentaries on the etiology, epidemiology, clinical characteristics, screening and testing. Clinical care and treatment and prevention and control.

  Rio and Malani (Feb 28, 2020). COVID-19—New Insights on a Rapidly Changing Epidemic. American Medical Association. https://jamanetwork.com/journals/jama/fullarticle/2762510

- This MMWR report provides an update on the current COVID-19 response including US cases, travelers to outbreak areas, airport screening, persons under investigations, lab testing, and repatriation flights from areas with substantial COVID-19 transmission. *Interim guidance is available at* https://www.cdc.gov/coronavirus/index.html

  Jernigan (Feb 28, 2020). CDC COVID-19 Response Team: CDC Morbidity and Mortality Weekly Report. Update: Public Health Response to the Coronavirus Disease 2019 Outbreak —United States, February 24, 2020. http://dx.doi.org/10.15585/mmwr.mm6908e1